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Economic Analysis of Prophylactic Pegfilgrastim in Adult Cancer Patients Receiving Chemotherapy

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ABSTRACT

Objectives: Neutropenia and its complications, including febrile neutropenia (FN), are a common side effect of cancer chemotherapy. Results of clinical trials showed that prophylactic use of granulocyte colony-stimulating factors (G-CSF) is effective in preventing FN. In this study, the cost effectiveness (measured as cost per quality-adjusted time [days]) of three treatment alternatives were evaluated: no G-CSF, filgrastim administered daily for 7–12 days after chemotherapy, and a pegylated form of G-CSF pegfilgrastim, administered once per cycle.

Methods: A cost-utility model based on standard clinical practice of treating FN with immediate hospitalization or with ambulatory treatment, from a societal perspective was developed. Direct medical cost estimates for hospitalization were derived from claims data reported by 115 US academic medical centers. Indirect medical costs, productivity costs, probabilities, and utilities are based on published literature. Results were subjected to sensitivity analyses and 95% confidence intervals are based on a Monte Carlo simulation.

Results: Mean estimated costs/day of hospitalization were $1984 (SD $1040, N = 24,687) for surviving patients and $3139 (SD $2014, N = 1437) for dying patients. Under baseline conditions, pegfilgrastim dominated both filgrastim and no G-CSF, with expected costs and effectiveness of $4203 and 12.361 quality adjusted life-days (QALDs) for no G-CSF, $3058 and 12.967 QALDs for pegfilgrastim, and $5264 and 12.698 QALDs for filgrastim.

Conclusions: This cost-utility analysis provides strong evidence that pegfilgrastim is not only cost-effective but also cost-saving in most common clinical and economic settings. There appear to be both clinical and economic benefits from prophylactic administration of pegfilgrastim.

Keywords: cancer, cost analysis, decision models, febrile neutropenia, granulocyte colony-stimulating factors, neutropenia.

Introduction

Neutropenia is a common chemotherapy-related complication. Neutropenia is defined as a below normal count of neutrophils (white blood cells), which are particularly important in fighting and preventing infection. Febrile neutropenia (FN), defined as the presence of both neutropenia and fever, routinely prompts immediate hospitalization for evaluation and administration of empirical broad-spectrum antibiotics [1] and may subsequently result in chemotherapy dose delays or reductions [2]. It is estimated that in the United States, more than 60,000 neutropenia-related hospitalizations occur each year [3]. The costs associated with those hospitalizations add significantly to the direct medical costs of cancer treatment and pose a great financial burden in the overall care of cancer patients [4].

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Considerable attention has been given in recent years to identifying FN patients at low risk of complications who may be candidates for outpatient treatment with antibiotics [5]. Although replacing hospitalization and intravenous (IV) antibiotic treatment with outpatient oral antibiotics holds promise for savings, a formal cost analysis of outpatient treatment demonstrated only limited economic effect on the overall cost of cancer treatment as low-risk patients account for a small proportion of the overall costs of cancer patient care for FN [6].

Randomized controlled trials (RCTs) have demonstrated that prophylactic granulocyte colony-stimulating factors (G-CSF; filgrastim) initiated after myelosuppressive chemotherapy and administered daily until neutrophil recovery is effective in reducing the incidence of FN by as much as 50% [7,8]. Patients treated with a G-CSF have shorter lengths of hospitalization (LOS) and shorter time to neutrophil recovery than control subjects [9]. Recently updated guidelines of the American Society of Clinical Oncology (ASCO) and the European Organization for Research and

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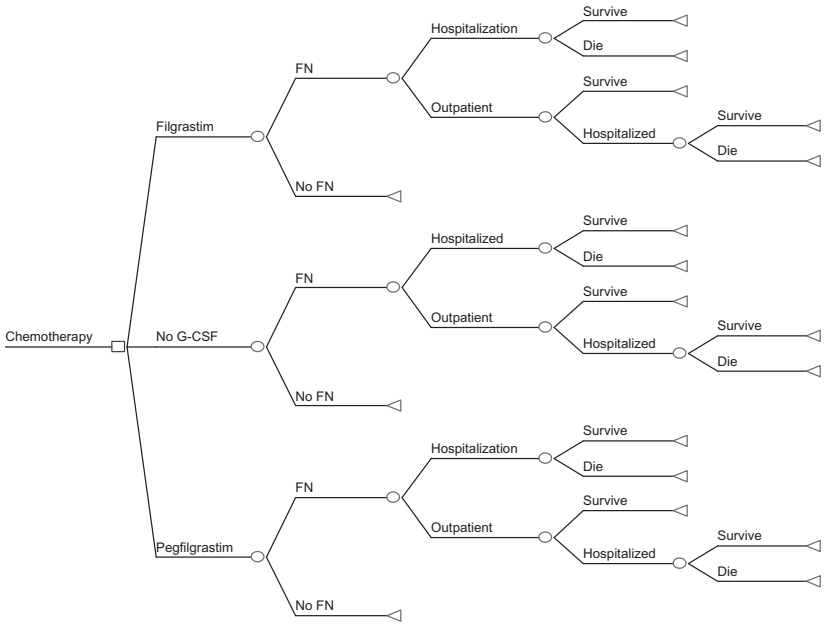

Figure 1 Clinical decision model for studying the effect of prophylactic use of pegfilgrastim or filgrastim on the expected costs of cancer treatment per patient in the first cycle, showing two standard clinical strategies. FN, febrile neutropenia; G-CSF, granulocyte colony-stimulating factors.

Treatment of Cancer (EORTC) recommend primary (first cycle) prophylactic G-CSF administration for chemotherapy regimens associated with an FN incidence rate of 20% or greater, or when special circumstances exist, such as history of recurrent FN or more advanced cancer [10–12].

A new, long-acting pegylated form of G-CSF, pegfilgrastim (Neulasta; Amgen Inc., Thousand Oaks, CA) administered once per chemotherapy cycle, has been shown in recent RCTs to be at least as effective and safe as filgrastim [13,14], demonstrating a relative risk reduction (RRR) for FN greater than 90% [15]. Because of its convenient administration to both the patient and medical staff and potentially increased effectiveness, pegfilgrastim often displaces filgrastim in the United States whenever it is being reimbursed by payers [16]. Many patients receiving conventional systemic chemotherapy are not receiving primary prophylaxis with G-CSF [2,17], suggesting that many physicians still consider "watchful waiting" a valid treatment option during the first cycle of chemotherapy.

Although the economic impact of filgrastim has been well studied, indicating that primary prophylaxis in patients receiving chemotherapy can be cost-effective compared with "no G-CSF" (attributed mainly to a decreased risk of FN) [18,19], and despite considerable clinical interest and wide-scale use of pegfilgrastim, a thorough economic evaluation of pegfilgrastim has not been previously reported. The objective of this analysis is to evaluate the economic impact of pegfilgrastim compared with filgrastim and no G-CSF when administered prophylactically during the first cycle of chemotherapy.

Methods

Decision Analysis

A cost-utility (CU) model was created to compare the economic impact of three treatment alternatives: primary prophylactic use of pegfilgrastim, primary prophylactic use of filgrastim, and no prophylactic G-CSF (Fig. 1). This model was premised on common clinical practice, in which patients receiving chemotherapy are at risk for developing FN. Patients experiencing FN are then managed either as inpatients or as outpatients based on their risk of serious complications or death. An outpatient treatment includes the administration of IV antibiotics and may be followed by hospitalization if the patient's condition deteriorates.

The modeled population consists of patients between the ages of 18 and 65 years old, hospitalized between 1995 and 2003 for a solid tumor cancer as identified by the International Classification of Disease, Ninth version, Clinical Modification (ICD-9-CM) codes 140.00 to 199.00, and also with a diagnosis of neutropenia (agranulocytosis), ICD-9-CM code 288.00. Costs and LOS were estimated for surviving and dying patients separately.

The analysis was performed from the societal perspective, incorporating direct as well as indirect medical costs, productivity costs, and travel costs (Table 1). Costs are measured in US dollars, adjusted to 2005 using the Consumer Price Index—Urban for medical care [29]. Effectiveness is measured in quality-adjusted life-days (QALDs). The time horizon is the first cycle of chemotherapy defined as 21 days, when most patients receive full-dose chemotherapy, often

Table 1 Summary of parameters used in decision analysis: numeric baseline values, parameter range used in sensitivity analyses, distribution type and parameters, and references

Model parameters	Baseline value	Range tested in sensitivity analysis	Distribution type and parameters*	References
Probabilities				
Incidence of FN	0.2	0.05–0.4	Point estimate	[15]
Hospitalization for FN	0.82	0.5–1	Beta, SD 0.04	[15]
Hospitalization for FN following outpatient treatment	0.16	0.1–0.5	Beta, SD 0.06	[20]
FN-related death, while outpatient treatment for FN	0	0–1	Point estimate	[15,20]
FN-related death, while hospitalized for FN	0.08	0.01–0.2	Beta, SD 0.03	[4]
RRR of FN associated with pegfilgrastim	0.9	0.5–1	Point estimate	[15,21]
RRR of FN associated with filgrastim	0.39	0.28–0.48	Point estimate	[21]
FN-related hospitalization	0.88	0.7–1	Beta, SD 0.03	[15]
Reduction in LOS associated with G-CSF	0.2	0–0.5	Point estimate	[9]
Time [unit of measurement]				
Hospital LOS for surviving patients (days)	9	1–30	Point estimate	UHC
Hospital LOS for dying patients (days)	15	1–30	Point estimate	UHC
FN as outpatient (days)	5	4–6	Uniform, SD 0.57	[22]
Number of filgrastim injection	8	7–12	Point estimate	[19]
Patient's time for IV antibiotic injection, outpatient (hours)	3.26	0.8–7.5	Gamma, SD 0.98	[23]
Patient's time for filgrastim injection, outpatient (hours)	2.32	0.45–4.3	Gamma, SD 0.87	[23]
Patient's time for pegfilgrastim injection (hours)	2.36	1.45–11.2	Gamma, SD 1.45	[23]
Costs (US$, 2005)				
IV antibiotics per injection†	36	15–100	Point estimate	[24]
Hospitalization per day for surviving patients	1971	1000–5000	Lognormal, SD 937.8	UHC
Hospitalization per day for dying patients	3128	1000–5000	Lognormal, SD 1977.8	UHC
Filgrastim, per injection†	282	207.5–362.6	Point estimate	[24]
Pegfilgrastim per injection†	2603	1500–4000	Point estimate	[24]
Physician cost/day	200	0–500	Point estimate	MedStat
Cost of medical staff per episode of outpatient IV antibiotics injection	91	39–162	Lognormal, SD 46.3	[22]
Cost of medical staff per episode of outpatient filgrastim injection	63.4	12–147	Lognormal, SD 31.73	[22]
Cost of medical staff per episode of outpatient pegfilgrastim injection	62.33	12–122	Lognormal, SD 33.53	[22]
Travel per outpatient visit/hospitalization	14	10–20	Point estimate	[25]
Patient's average hourly wage	18	12–20	Lognormal, SD 15.7	[26]
Utilities				
Cancer with chemotherapy treatment	0.62	0.4–0.84	Point estimate	[27]
Infection without hospitalization	0.48	0–1	Point estimate	[27]
FN with hospitalization	0.24	0.12–0.36	Point estimate	[27]
Difference in utility attributed to G-CSF‡	0	(–0.2)–0.2	Point estimate	[28]

*Mean is as specified in baseline value, unless otherwise specified.
†Cost presented incorporates 15% discount, reflecting average institutional discount below average wholesale price.
‡Range is based on assumption.
The information contained in this article was based in part on the Clinical Data Products Database maintained by the University HealthSystem Consortium (UHC).
FN, febrile neutropenia; G-CSF, granulocyte colony-stimulating factors; IV, intravenous; IRM, infection-related mortality; LOS, length of stay; RRR, relative risk reduction.

without G-CSF prophylaxis [30] and because the occurrence of FN during the first cycle of chemotherapy is shown to be a good predictor of neutropenic events in subsequent cycles [31]. The model was constructed using decision analysis computer software TreeAge Pro2005 (TreeAge Software Inc., Williamstown, MA).

Probabilities

Probabilities including incidence of FN, hospitalization for FN, mortality, and RRR of filgrastim and pegfilgrastim were based on the published literature [4,9,15,21]. Several studies are available describing the use of IV antibiotics in the outpatient setting in terms of both efficacy and duration of treatment [5,20,22,32]. Based on those studies, our base case analysis assumes no FN-related deaths occur in outpatient settings, because these patients are highly selected low-risk patients. Probability of hospitalization among those initially treated as outpatients and who subsequently developed more severe symptoms requiring hospitalization is based on Talcott [20]. The model assumes that if such hospitalizations are needed, they occur half way through outpatient treatment. Baseline probabilities, their ranges tested in sensitivity analyses, and references are presented in Table 1.

Cost Estimates

The University HealthSystem Consortium (UHC) is a database incorporating information from 115 academic medical centers and 149 of their affiliated hospitals, representing approximately 90% of US nonprofit academic medical centers. The data set includes clinical as well as administrative information designed primarily to provide participating hospitals with the needed information to improve their performance. Average hospitalization costs were estimated for each participating institution within the UHC from detailed hospital charges collected at the revenue code level and mapped into individual departments. Departmental

costs were estimated from reported charges by multiplying the department charge by trimmed mean cost-to-charge ratios. Total hospitalization costs per patient were computed by summing individual cost center estimates.

Physician costs per day were based on validated patient-level data from commercial, Medicare and Medicaid claims (MarketScan: http://www.medstat.com) provided on some 7 million covered lives by large employers, nationwide plans including Blue Cross/Blue Shield, third-party administrators, and patients with primary coverage or Medicare Supplemental coverage through privately insured fee-for-service, point of service, or capitated health plans. This data set has been validated and used in both cancer and noncancer studies [33,34]. Outpatient medical staff costs were based on a study carried out by Fortner et al. [22], in which the researchers measured time and costs for various human resources, including both medical and nonmedical services necessary to manage chemotherapy, chemotherapy-induced neutropenia, and administration of IV antibiotics in 20 community oncology practices in the United States. Prices of pegfilgrastim (6 mg), filgrastim (300 μg and 480 μg), and IV antibiotics (ceftazidime, 2 g) were obtained from the 2005 Drug Topics Red Book [24], discounted 15% of their average wholesale price to reflect institutional contract prices. At baseline, the model assumes that in outpatient settings, pegfilgrastim was administered once per cycle, filgrastim was administered in clinic for eight consecutive days, and IV antibiotics were administered once a day, for 5 days.

Patient time spent on treatment was valued using measures of patients' time spent on clinic visits, including their travel time to and from the clinic [23]. Each day of hospitalization was assumed to cause the loss of 8 hours of paid work. Average hourly earnings are based on data collected by the US Department of Labor, Bureau of Labor Statistics, 2004 for all occupations [26]. The cost of round-trip travel was valued at $14 per outpatient visit or hospitalization, based on the standard mileage rate for calculating tax-deductible travel [25] and an assumption that each patient had to travel 35 miles per visit. We did not account for out-of-pocket expenses. Baseline costs and their ranges tested in sensitivity analyses are presented in Table 1.

Health Outcome

QALDs were estimated from the duration in a given health state, adjusted by the appropriate preference-based quality weight (utilities) associated with the health state. Utilities for the three health states represented in the model—stable disease, FN with hospitalization, and FN without hospitalization—were derived from a study where 180 nurses served as proxies in evaluating cancer patients' preferences, using the standard gamble method. Health states were defined without specification of chemotherapy regimens or cancer type and hence could be applied to our modeled population [27]. Limited data from available trials exploring the impact of G-CSF on patients' quality of life or survival have failed to demonstrate a significant difference between the two strategies [28,35]. Therefore, it is assumed at baseline that health state utilities do not vary among the three treatment arms, and any variation in QALDs will result from differences in the duration spent in each state. Utilities were varied in a sensitivity analysis to compare the impact on the different treatment strategies. Utilities and time spent in each health state, as well as their ranges tested in sensitivity analysis are presented in Table 1.

Sensitivity Analyses

One-way sensitivity analysis was performed for each parameter in the model over a clinically or economically plausible range of values (Table 1). Because estimates of RRR for filgrastim and pegfilgrastim are based on different RCTs, we tested the assumption of no difference in RRR between the two treatments with a combined RRR value of 0.53 compared with no G-CSF, based on a meta-analysis combining all studies [21].

To provide a more comprehensive examination of the uncertainty in the model parameters and assumptions and to establish an empirical distribution of the results of the study, a probabilistic sensitivity analysis was conducted using a second-order Monte Carlo simulation. The simulation was conducted based on 5000 iterations providing 95% confidence intervals for the mean incremental cost-effectiveness ratio (ICER), by sampling values from all parameter distributions. Estimates of mean costs approximated a log-normal distribution, while probabilities and incidences were assumed to follow a beta distribution and estimates of mean patient time were assumed to follow a gamma distribution [36].

Results

Costs and Length of Stay Analysis

Cost data were available on 24,687 patients surviving hospitalization with FN and 1437 patients dying during the course of FN hospitalization. The mean (SD) and median estimated hospitalization costs per day were $1984 ($1040) and $1717, respectively, for surviving patients and $3139 ($2014) and $2545 for dying patients. Distributions for both groups followed the log-normal distribution. Average hospitalization LOS was 9 days (range 1–30 days) in surviving patients and 15 days (range 1–30 days) for patients who died.

Table 2 Incremental cost effectiveness analysis comparing treatment alternatives

Intervention	Cost ($US, 2005)	Effectiveness (QALDs)	Incremental cost (ΔC)	Incremental effectiveness (ΔE)	Incremental cost-effectiveness ratio (ΔC/ΔE)
Pegfilgrastim	3057	12.967	—	—	
No G-CSF*	4185	12.362	1128	–0.606	Dominated
Filgrastim*	5252	12.698	2195	–0.269	Dominated

*Compared with pegfilgrastim.
G-CSF, granulocyte colony-stimulating factor; QALD, quality-adjusted life days.

Baseline Analysis

Under baseline conditions, pegfilgrastim dominated both no G-CSF and filgrastim because it was the least costly and most effective (Table 2). Mean costs (savings) associated with pegfilgrastim were ($1128) compared with no G-CSF and ($2195) compared with filgrastim. Mean difference in effectiveness was 0.606 QALD and 0.269 QALD, respectively.

Sensitivity Analyses

Univariate sensitivity analyses were conducted for all model parameters over the ranges of values specified in Table 1. Results of sensitivity analyses for RRR of filgrastim, cost of IV antibiotics, LOS for dying patients, cost/day of dying patients, and cost of IV antibiotics were robust to value changes.

The effect of varying the probability of FN demonstrates that pegfilgrastim dominates both alternatives at values greater than 14%; under lower values it will be more costly and more effective than no G-CSF (with ICER of $11,616/QALD at the lowest probability value of 5%) and continue to dominate filgrastim. Similarly, varying RRR of pegfilgrastim demonstrates a cost-neutral threshold at an RRR = 0.56; at higher values, pegfilgrastim dominates both alternatives, and at lower values it dominates filgrastim but is more costly and more effective than no G-CSF (with ICER of $534/QALD at lowest RRR value of 0.5). Varying the cost of pegfilgrastim shows that only for prices higher than $3700 prophylactic pegfilgrastim strategy results in a net increase in cost compared with no G-CSF (ICER of $444/QALD when the cost is $4000). Thresholds for LOS and cost/day of surviving patients under which pegfilgrastim dominates both arms are N = 6 and cost/day = $1100 (with ICER of $11,295/QALD for N = 1 and ICER of $315/QALD for cost/day = $1000), respectively. Varying the difference in utilities between G-CSF arms and no G-CSF shows that even if G-CSFs are 4% less effective than no G-CSF (i.e., G-CSF has lower utility values), pegfilgrastim still dominates. If G-CSF results in utility decreases greater than 4%, no G-CSF becomes the most effective strategy.

Testing the assumption of equal RRR of both filgrastim and pegfilgrastim at a value of 0.53 showed that pegfilgrastim still dominated its alternatives. It was the least costly with incremental cost (savings) of ($23) and ($487) compared with no G-CSF and filgrastim, respectively. Pegfilgrastim was equally effective as filgrastim but more effective than no G-CSF, creating additional 0.43 QALDs.

Results from Monte Carlo simulation show mean (SD) expected costs and effectiveness for no G-CSF arm to be $4203 ($1462) and 12.361 QALDs (0.022), for the pegfilgrastim arm $3058 ($123) and 12.967 QALDs (0.001), and for the filgrastim arm $5264 ($772) and 12.698 QALDs (0.01). The lower SD demonstrated in the cost of the pegfilgrastim arm is attributed mainly to the reduction in the incidence of FN, thus compressing the high-risk values (and their related expected costs) toward the goal of no FN risk. Figure 2 shows two scatter plots of ICERs: the scatter plot of ICERs of pegfilgrastim compared with no G-CSF demonstrates that no G-CSF is less effective in all iterations but is more costly in about 80% of iterations, and the scatter plot of ICERs of pegfilgrastim

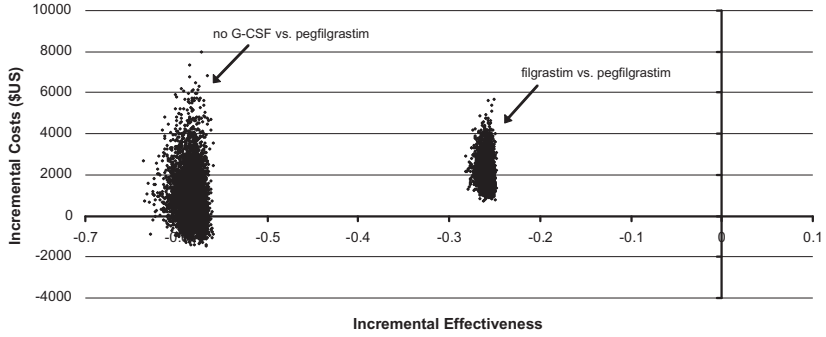

Figure 2 Results of Monte Carlo simulation showing two groups of scatter plots in the cost-effectiveness plane: incremental cost-effectivneess ratio of no G-CSF versus pegfilgrastim and filgrastim versus pegfilgrastim.

compared with filgrastim demonstrates that the ICERs fall within the upper left quadrant of the cost-effectiveness plane at all iterations.

Discussion

In the study reported here, a decision analytic model was used to conduct a CU analysis of primary prophylaxis pegfilgrastim compared with primary prophylaxis filgrastim and to no prophylactic G-CSF in cancer patients receiving systemic chemotherapy. Two common clinical practices for treating FN were considered: immediate hospitalization or ambulatory treatment followed by hospitalization, if needed. The results of the model suggest that despite the added cost of pegfilgrastim, the overall cost of care is reduced when pegfilgrastim is used prophylactically with chemotherapy regimens associated with approximately a 16% or greater risk of FN. Monte Carlo simulation suggests that prophylactic pegfilgrastim is associated with an actual cost savings in approximately three-quaters of patients receiving prophylactic pegfilgrastim compared with patients without prophylactic G-CSF, and with increases in QALDs whenever G-CSFs are used. These cost savings and increased effectiveness are primarily due to the reduction in hospitalization for FN along with a reduction in severity of FN, allowing for shorter hospitalization. The results reported here, in addition to the compelling evidence for clinical benefit from several RCTs, are consistent with current recommendations of ASCO guidelines to use prophylactic pegfilgrastim when the risk of FN is 20% or greater.

In the model presented here, the two comparison groups shown in Figure 2 fall within two quadrants of the cost-effectiveness plane; no G-CSF versus pegfilgrastim falls within the upper left and lower left quadrants, indicating that about 80% of the joint density is associated with cost savings for pegfilgrastim with all of the contrasts yielding gains in QALDs for pegfilgrastim. Filgrastim versus pegfilgrastim falls only within the upper left quadrant, indicating that pegfilgrastim is always less expensive and more effective than filgrastim. These results are relatively unique because in the current cost-effectiveness literature, only a small fraction of reported interventions are actually cost-saving [37]. Moreover, even in the 20% of iterations where pegfilgrastim was more expensive, it may still be cost-effective. As with other interventions, if they indeed provide improved health, it may be reasonable to have net increases in cost associated with them.

The analysis presented here is focused on the first cycle of chemotherapy for two reasons: first, it is the first cycle when most patients receive full-dose chemotherapy generally without growth factor prophylaxis. As a result, the first cycle of chemotherapy has been consistently associated with a greater risk of FN than subsequent cycles. Parameter estimates change little over multiple cycles, unless there is a change in delivered dose intensity or the addition of G-CSF. Therefore, in settings where maintaining chemotherapy dose intensity is thought to be important for disease control, subsequent cycles of chemotherapy administered at full-dose intensity will be accompanied by the same or greater risk of FN unless growth factors are administered prophylactically. Second, the majority of patients experiencing neutropenia or its complications in the first cycle also experience dose reductions, treatment delays, or the addition of G-CSF on subsequent cycles and, as a result, FN episodes in successive cycles may be related.

Recent studies have demonstrated that prophylactic antibiotics may also reduce the risk of FN among patients receiving chemotherapy, especially among those with hematologic malignancies [38,39]. Nevertheless, prophylactic antibiotics do not address the underlying neutropenia and are not currently recommended by any medical professional society because of evidence that such treatment may increase the risk of developing antibiotic resistance [1,10]. In addition, a recent randomized phase III trial investigating the role of adding primary prophylaxis G-CSF to antibiotic prophylaxis in small-cell lung cancer demonstrated that the incidence of FN was further reduced during the first cycle with G-CSF (24% vs. 10%, $P = 0.01$), and as noted previously, the risk of FN was the highest during the first cycle and decreased substantially in subsequent cycles [32]. These findings emphasize the importance of the first cycle of chemotherapy and the role of preventing FN during this cycle as discussed above.

The model presented here has several limitations. The baseline model combines estimates of FN, RRR of filgrastim, and RRR of pegfilgrastim from clinical trials. Those studies differ in their chemotherapy regimen, creating different baseline risk levels of FN. Because the association between baseline risk of FN and clinical effectiveness of G-CSF is not fully determined, the baseline results may vary. Using a RRR of filgrastim, which is a weighted summary across different chemotherapy regimens as calculated in a meta-analysis, should reduce the potential variability. The estimates of RRR for pegfilgrastim are also based on the meta-analysis but include only one published RCT [15,21]. This multicenter, multinational study, however, represents the largest RCT of a myeloid growth factor reported to date. Moreover, as the sensitivity analyses show, even when varying the values mentioned above across their plausible clinical values, or when equating their clinical effectiveness (i.e., RRR), pegfilgrastim remains dominant under most values.

Although it is estimated that more than half of cancer patients in the United States are older than

65 years, the modeled population is defined as patients between 18 and 65 years of age, which limits the generalizability of the model. The fact that the study population was limited to the 65-years-and-less age group permitted a better definition of the costs incorporated into the model (e.g., productivity cost, a component of which would be problematic to estimate when dealing with elderly population). In addition, comorbidities among different age groups may vary, implicating great variability in length and costs of hospitalization. The meta-analysis of RCTs of prophylactic G-CSF used to estimate RRRs incorporates data from 17 RCTs in adult cancer patients, including six that excluded elderly patients more than 65 years of age, four that included only patients older than the age of 60, and the rest, which allowed patients of all ages. No significant difference in clinical efficacy among different age groups was found. By specifying the defined study population considered here, the accuracy of "real-world" costs based on our model should be increased.

Another limitation of the model is the derivation of hospitalization cost per day from an administrative data set of hospitalization charges of academic hospitals. Although the charges are adjusted based on a department-specific cost-to-charge ratio to appropriately address the societal perspective our analysis takes, the estimates may still be somewhat higher than when treating FN in a nonacademic hospital.

Further analysis that takes into consideration a longer time horizon and the potential long-term effects of pegfilgrastim and filgrastim on chemotherapy dose reductions or delays and survival should be undertaken. The model presented here compares only two treatment alternatives—prophylactic G-CSF (either filgrastim or pegfilgrastim) versus no G-CSF at all—and does not consider the cases where patients are given G-CSF only secondarily after already presenting to the hospital with FN. Our estimates of FN risk and hospitalization while using pegfilgrastim or filgrastim are based largely on evidence from RCTs. These trials are designed primarily to test the safety and efficacy of a treatment, and are usually restricted to highly selected patients, leading to a potential bias when applying results to the general disease population. Nevertheless, estimates of infection-related mortality in the control arm of the RCTs were similar to those reported in cohort or observational studies of cancer patients experiencing FN [4].

This analysis provides evidence that pegfilgrastim is not only cost-effective but, in most cases, also cost-saving across a wide range of estimates of clinical and economic values. Therefore, in addition to compelling evidence for considerable clinical benefit with moderately myelosuppressive regimens, primary prophylaxis with pegfilgrastim reduces costs in settings where maintaining treatment dose intensity is considered important to providing patients with optimal long-term disease control or cure.

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